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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/720,513	03/26/2001	Therese Jourdier	MBHB00-1282	3546

20306 7590 03/13/2002

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	4

DATE MAILED: 03/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/720,513	JOURDIER ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims are 10-15 are pending.

Preliminary Amendment is acknowledged. Claims 1-9 are canceled and new claims 10-15 are added. Claims 10-15 are considered before the examiner.

Specification

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 10-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 is indefinite in that the metes and bonds of " an immunogen" and "a pathogen agent" are not defined. Although the claim is interpreted in light of the specification, the limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Moreover, because there are so many immunogen and pathogen in the art, the claim should point out which immnugen and pathogen are intended in the said claim. This affects the dependent claims 12-15.

Claim 10 is also unclear in that metes and bonds of a systemic response are not defined. Although the claim is interpreted in light of the specification, the limitations from the specification are not read into the claims; however, the specification fail to define what the definition of a human systemic response is. This affects the dependent claims 12-15.

Claims 10-15 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: what kind of the immunogen is used, what kind of

a human systemic response is measured and what concentration of the composition comprising the immnnunogen is applicable etc.

Claim Rejections - 35 USC § 112

Claims 10-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for sensitizing the B lymphocytes isolated from the located lymph nodes , such as internal or external iliac lymph nodes, inguinal lymph nodes in an ex vivo experiments and getting some secreted IgA in the rectal, genital and/or urinary wash by injecting an immuneogenic composition comprising the HIV gp120 and gp160 intramuscularly into the thigh of mice, does not reasonably provide enablement for inducing similar immune response in human by injecting any or all immunogen for any or all pathogen agent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and gain in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988). These factors include the following:

1) &2). State of art and Unpredictability of the field.

State of art teach that the immunogenic composition can be injection in variety routes , such as intramuscularly or intravenously or subcutaneous, into a host to induce an immune response (See Stites et al. Medical Immunology, Edited by Stites et al. 9th edition, 1997, published by Applenton & Lange, Stanford, Connecticut. See the section of Technique of immunization on page 782 and Table 55-2 from pages 774-781.).

However, whether all immunogen isolated injected intramuscularly away from the mucus region can produce a significant immunity is unpredictable as evidenced by Hartman et al. They teach that the distant delivery of an immunogenic composition by muscular injection of O-antigen-protein did not protect naive animal against the subsequent challenge of the pathogen

(INFECTION AND IMMUNITY 1994M Vol. 62, pp. 412-420. See abstract). Whether every antigen can produce a strong mucosal IgA immunity by muscle injection is also unpredictable as evidenced by Onien et al. (Vaccine 1994, Vol. 12, pp. 731-735). They teach that a respiratory syncytial virus (RSV) chimeric FG glycoprotein does not induce local IgA and IgG antibodies production by a parental route (See abstract), indicating that different antigen has different properties and they may behave differently in turn of inducing a protective immunity through different route of the immunization.

3) & 4) Number of working examples and amount of guidance presented.

Applicants only present the B cell isolated from the regional lymph nodes near the injection site, can be sensitized strongly in an in ex vivo experiment or IgA can be secreted in the regional mucosal near the injection site after injection of the DNA construct encoding the HIV gp160. Applicants has not shown that the injection of any or all immunogen of any or all pathogen as listed in claim 14 can produce a similar immune response in a human body.

Applicant does not teach any or all immunogen from any or all pathogens listed in claim 14, can induce a systematic as well as local immunity though the intramuscularly injection at the thigh of a human being.

Furthermore, Applicants fail to teach or provide an guidance that what kind of the immunogen is suitable for doing intramuscularly injecting, which is enable to induce a systemic as well as local immune response by intramuscularly injection.

Applicants are reminded that the result of the in vitro data or a small animal model cannot extrapolated into the result in vivo.

5) Scope of the claims.

The claims read broadly on any or all imunogen of any or all pathogen that can induce a systematic as well as local immunity in human by an intramuscularly injection at the thigh site of a human body.

6) & 7) Nature of the invention and lever of the skill in the art.

The invention involves one of the most complex and unpredictable field of vaccine development. A significant hurdles remain to be overcome in order for the skilled artisan to practice successful the full scope of the claimed invention.

Given the above analysis of the factors, which the courts have determined, are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan would have had to conduct undue and excessive experimentation in order to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 10-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Morrow et al. (US Patent No. 6,063,384A).

Morrow et al. teach a method for stimulating an immune response to an immunnogenic protein by intramuscularly injection of the composition, wherein the composition is selected from the group consisting of the gag protein, the pol protein and the eve protein of HIV-1 (Claims 1-10). Because the thighs belong to the muscle, the claimed invention is, therefore, anticipated by the cited reference.

Claims 10-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Whittle et al. (US Patent NO. 6,123,948A).

Whittle et al. teach a method for stimulating an immune response to an immunnogenic protein by intramuscularly injection of the composition comprising human papilloma virus protein L2E7 fusion protein into the human volunteers. Because the thigh belongs to the muscle, the claimed invention is, therefore, anticipated by the cited reference.

Claims 10-15 are rejected under 35 U.S.C. 102(e) as being anticipated by Krieg et al. (US Patent NO. 6,339,068B1).

Krieg et al. teach a method for stimulating an immune response to an immunnogenic protein by intramuscularly injection of the composition comprising human viral antigen with

CpG motif of the immune stimulatory sequence, wherein the viral antigen include the herpes simple virus antigen (line 25, col. 14). Krieg et al. especially teach the advantage of the intramuscularly injection of the vaccine in that muscle cell can be efficiently transfected to express some B-cell epitope, which may not present by the antigen presenting cell (APC). Thus, when strong humoral immune responses are desired, the injection of the DNA vaccine with a strong muscle-specific promoter, is more preferable (Lines 8-32 on col. 8). Because the thigh belongs to the muscle, the claimed invention is, therefore, anticipated by the cited reference.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 10-15 are rejected under 35 U.S.C. 102(a) as being anticipated by Cohen et al. (US Patent No. 5,654,174A, August 5, 1997).

Cohen et al. disclose variant Herpes simplex virus type-1 (HSV-1) glycoprotein (gD) and type-2 gD that are capable of prevent the infection of cells by HSV-1 and HSV-2. They also teach that the gD variant molecules are administered to the mammal, especially human, in an amount sufficient by variety routs including an intramuscularly injection (See lines 57 of col. 3 through line 27 of col. 4). Because the thigh belongs to the muscle, the claimed invention is, therefore, anticipated by the cited reference.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Carrano et al. (WO 95/26718A1).

Carrano et al. disclose method for introducing a genetic construct into a an individual by the intramuscularly or skin injection, wherein the construct encodes a pathogen selected form variety of viruses, including HIV, human pappiloma virus (HPV), herpes simplex 1 virus type I and 2 etc (claims 18-19). The delivery of the gene constructs, which encode target proteins, can confer mucosal immunity. Because the thigh belongs to the muscle, the claimed invention is, therefore, anticipated by the cited reference.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over McBride et al. (Vaccine 1988, Vol. 6, pp. 414-418) and Lehner et al. (J. Immunol. 1994, Vol. 15, pp. 1858-1868).

McBride et al. teach a method for inducing a protective immune response against HSV by vaccinating the female guinea-pig subcutaneous at the distant site. They found that the HSV specific antibodies, including the IgG and IgA are detected in both serum and vaginal wash. They concluded that the Skinner vaccine prepared in Alhudrogel injected subcutaneous in the distant, is capable of generating memory mucosal immunity in the guinea-pig vaginal mucosa. Although they did not teach that vaccination is done by intramuscularly injection in human, they disclose that 50 human volunteers at high risk of contracting herpes genitals, immunized with the said vaccine preparation, also demonstrate a good protection against the primary disease. They also suggested that since serum antibody does not prevent recurrent infection, the production of local immunity, mediated by both T and B cells, will be important aspects to investigate in any potential herpes vaccine. McBride et al. does not teach other sexual transmitted disease, such as HIV-1, can be protected by the similar.

Lehner et al. teach a protective mucosal immunity is elicited by injecting the vaccine consisting of rSIV protein p27 administered in the proximity of the internal iliac lymph nodes. The secretory IgG and IgA abs to p27 Ag were elicited in the virginal, male urethral, rectal and seminal fluids, urine and serum. They conclude that generating secretory IgA and IgG Abs at the mucosal surface, and T and B cell immunity in regional draining lymph nodes, spleen and circulation may prevent the virus through the mucosa, dissemination of virus, and the formation of a latent reservoir of infection (See entire document).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited references to administering the antigen of many other sexual transmitted disease, which are identified in the art so far, into the proximity of the rectal and/congenital mucosal region and see the immune response with highly expected result. It is the examiner's position that the routs of the injection whether the injection is intramuscularly or subcutaneous are just the design choice as long as the injection is near the internal iliac lymph nodes or near the rectal and congenital area as disclosed by Lehner et al. and McBride et al. As there are no unexpected results have been provided, the claimed invention as a whole is prima facie obvious absence unexpected results.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 8:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li

March 8, 2002

ALI R. SALIMI
PRIMARY EXAMINER